

In re Appln. of ALAM et al.  
Application No. 10/034,432

*CLAIM AMENDMENTS*

1. (Currently Amended) An aqueous indocyanine green (ICG) composition comprising ICG at a concentration of at least about [10] 20 mg/ml and an aqueous diluent comprising a solubilizer and an alcohol, wherein the composition exhibits a loss of ICG potency of less than about 10% [is stable] for at least 24 hours when stored in a 25°C environment.

2. (Currently Amended) The aqueous ICG composition according to claim 1, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

3. (Currently Amended) The aqueous ICG composition according to claim 2, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 5 days.

Claim 4 (Canceled)

5. (Currently Amended) The aqueous ICG composition according to claim [4] 1, wherein the ICG concentration is at least about 50 mg/ml.

6. (Currently Amended) The aqueous ICG composition according to claim 5, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 5 days.

7. (Currently Amended) The aqueous ICG composition according to claim 6, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least one week.

8. (Original) The aqueous ICG composition according to claim 5, wherein the ICG concentration is at least about 75 mg/ml.

9. (Currently Amended) The aqueous ICG composition according to claim 8, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 24 hours.

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10. (Currently Amended) The aqueous ICG composition according to claim 9, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least three days.

11. (Currently Amended) The aqueous ICG composition according to claim 10, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least one week.

12. (Original) The aqueous ICG composition according to claim 1, wherein the aqueous diluent comprises, per ml of diluent, about 0.5 to about 5 mg solubilizer and about 50 to about 150 mg alcohol, and wherein the composition has a pH of about 6 to about 8.

13. (Original) The aqueous ICG composition according to claim 12, wherein the solubilizer is a surfactant.

14. (Original) The aqueous ICG composition according to claim 13, wherein the alcohol is ethanol, propylene glycol, glycerine, or mixtures thereof.

15. (Original) The aqueous ICG composition according to claim 14, wherein the solubilizer is a nonionic surfactant.

16. (Original) The aqueous ICG composition according to claim 12, wherein the aqueous diluent further comprises, per ml of diluent, about 10 to about 100 mg polyvinyl pyrrolidone.

17. (Currently Amended) The aqueous ICG composition according to claim 16, wherein the aqueous diluent further comprises an antimicrobial in an amount [effect] effective to inhibit microbial growth in the aqueous ICG composition for at least one week.

18. (Original) The aqueous ICG composition according to claim 17, wherein the aqueous diluent comprises, per ml of diluent, about 1 to about 3 mg surfactant, about 75 to about 125 mg alcohol, about 25 to about 75 mg PVP, and wherein the pH of the diluent is about 6.5 to about 7.5.

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19. (Original) The aqueous ICG composition according to claim 12, wherein the ICG and aqueous diluent are segregated within a multi-chambered vessel prior to formation of the aqueous ICG composition.

20. (Original) The aqueous ICG composition according to claim 19, wherein the multi-chambered vessel is a dual-chamber syringe.

21. (Original) The aqueous ICG composition according to claim 19, wherein the multi-chambered vessel is a vial.

22. (Original) The aqueous ICG composition according to claim 1, wherein the ICG is provided as a sterile lyophilizate.

23. (Original) The aqueous ICG composition according to claim 22, wherein the composition is a liposomal ICG composition.

24. (Currently Amended) A method for providing an aqueous indocyanine green (ICG) composition comprising diluting ICG with an aqueous diluent comprising a solubilizer and an alcohol to provide an aqueous composition of ICG at a concentration of at least [10] 20 mg/ml, wherein the aqueous ICG composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 24 hours when stored in a 25°C environment.

25. (Original) The method according to claim 24, wherein the ICG is lyophilized prior to dilution with the aqueous diluent.

26. (Original) The method according to claim 24, wherein the ICG and aqueous diluent are segregated within a multi-chambered vessel prior to diluting the ICG with the aqueous diluent.

27. (Original) The method according to claim 26, wherein the multi-chambered vessel is a dual-chamber syringe.

28. (Original) The method according to claim 26, wherein the multi-chambered vessel is a vial.

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29. (Currently Amended) The method according to claim 24, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

30. (Currently Amended) The method according to claim 29, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 5 days.

Claim 31 (Canceled)

32. (Presently Amended) The method according to claim [31] 24, wherein the ICG concentration is at least about 50 mg/ml.

33. (Currently Amended) The method according to claim 32, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 5 days.

34. (Currently Amended) The method according to claim 33, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least one week.

35. (Original) The method according to claim 32, wherein the ICG concentration is at least about 75 mg/ml.

36. (Currently Amended) The method according to claim 35, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 24 hours.

37. (Currently Amended) The method according to claim 36, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least three days.

38. (Currently Amended) The method according to claim 37, wherein the composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least one week.

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39. (Original) The method according to claim 24, wherein the aqueous diluent comprises, per ml of diluent, about 0.5 to about 5 mg solubilizer and about 50 to about 150 mg alcohol, and wherein the composition has a pH of about 6 to about 8.

40. (Original) The method according to claim 39, wherein the solubilizer is a surfactant.

41. (Original) The method according to claim 40, wherein the alcohol is ethanol, propylene glycol, glycerine, or mixtures thereof.

42. (Original) The method according to claim 41, wherein the solubilizer is a nonionic surfactant.

43. (Original) The method according to claim 39, wherein the aqueous diluent further comprises, per ml of diluent, about 10 to about 100 mg polyvinyl pyrrolidone.

44. (Original) The method according to claim 43, wherein the aqueous diluent further comprises an antimicrobial in an amount effect to inhibit microbial growth in the aqueous ICG composition for least 7 days.

45. (Original) The method according to claim 44, wherein the aqueous diluent comprises, per ml of diluent, about 1 to about 3 mg surfactant, about 75 to about 125 mg alcohol, about 25 to about 75 mg PVP, and wherein the pH of the diluent is about 6.5 to about 7.5.

46. (Original) The method according to claim 24, wherein the ICG is provided as a lyophilizate.

47. (Original) The method according to claim 46, wherein the lyophilizate further comprises components which, when water is added, provide liposomal ICG.

48. (Currently Amended) A multi-chambered vessel comprising indocyanine green (ICG) is a first chamber and an aqueous diluent comprising a solubilizer and an alcohol in a second chamber, wherein the diluent, when mixed with the ICG, provides an aqueous composition having an ICG concentration of at least [10] 20 mg/ml and [stability of] exhibits

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composition having an ICG concentration of at least [10] 20 mg/ml and [stability of] exhibits a loss of ICG potency of less than about 10% for at least 24 hours when stored in a 25°C environment.

49. (Original) The multi-chambered vessel according to claim 48, wherein the vessel is a dual-chamber syringe.

50. (Original) The multi-chambered vessel according to claim 49, wherein the first chamber of the syringe comprises ICG as a lyophilizate.

51. (Original) The multi-chambered vessel according to claim 49, wherein the multi-chambered vessel is a vial.

52. (Currently Amended) A method of obtaining an angiographic image of tissue in a patient comprising administering an aqueous ICG composition comprising ICG at a concentration of at least about [10] 20 mg/ml and an aqueous diluent comprising a solubilizer and an alcohol to a patient; applying energy of a type and in an amount sufficient to cause ICG in the patient to fluoresce; and obtaining an angiographic image of the tissue while the ICG fluoresces, wherein the aqueous ICG composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 24 hours when stored in a 25°C environment.

53. (Original) The method of claim 52, wherein the energy is administered using an endoscope.

54. (Original) The method of claim 52, wherein the angiographic image is of tissue that defines a body cavity.

55. (Original) The method of claim 53, wherein the tissue is the eye, lung, gastrointestinal tract, bladder, pancreas, gall bladder, sinus, trachea, liver, kidney, heart, cervix, brain, ovary, prostate, stomach or skin.

56. (Original) The method according to claim 52, wherein the ICG is in the aqueous ICG composition at a concentration of at least 50 mg/ml.

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57. (Currently Amended) The method according to claim 56, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

58. (Currently Amended) The method according to claim 57, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

59. (Original) The method according to claim 53, wherein the ICG is in the aqueous ICG composition at a concentration of at least 75 mg/ml.

60. (Currently Amended) The method according to claim 59, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

61. (Currently Amended) The method according to claim 59, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

62. (Original) The method according to claim 52, further comprising applying radiation of a type and in an amount effective to provide photodynamic therapy to the patient.

63. (Original) The method according to claim 62, wherein the radiation effective to provide photodynamic therapy is administered by an endoscope.

64. (Original) The method according to claim 63, wherein the ICG is provided at a concentration of at least 25 mg/ml.

65. (Original) The method according to claim 64, wherein the ICG is provided at a concentration of at least 50 mg/ml.

66. (Currently Amended) A method for diagnosing and treating a lesion in an animal, wherein a blood vessel feeds blood into the lesion, comprising

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- (a) administering an aqueous ICG composition comprising ICG at a concentration of at least about [10] 25 mg/ml and an aqueous diluent comprising a solubilizer and an alcohol to a patient;
- (b) applying energy of a type and in an amount sufficient to cause the ICG to fluoresce as the ICG flows through the blood vessels;
- (c) obtaining an angiographic image of the fluorescing ICG dye as the dye flows through the blood vessels;
- (d) analyzing the angiographic image obtained in step (c) to determine the presence of a lesion; and
- (e) applying energy to the blood vessel feeding blood into the lesion of a type and in an amount sufficient to reduce the rate of rate of blood flow through the blood vessel, wherein the aqueous ICG composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 24 hours when stored in a 25°C environment.

67. (Original) The method of claim 66, wherein the energy is administered using an endoscope.

68. (Original) The method of claim 66, wherein the angiographic image is of tissue that defines a body cavity.

69. (Original) The method of claim 68, wherein the tissue is the eye, lung, gastrointestinal tract, bladder, pancreas, gall bladder, sinus, trachea, liver, kidney, heart, cervix, brain, ovary, prostate, stomach or skin.

70. (Original) The method according to claim 66, wherein the ICG is in the aqueous ICG composition at a concentration of at least 50 mg/ml.

71. (Currently Amended) The method according to claim 70, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

72. (Currently Amended) The method according to claim 71, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

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73. (Original) The method according to claim 66, wherein the ICG is in the aqueous ICG composition at a concentration of at least 75 mg/ml.

74. (Currently Amended) The method according to claim 73, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

75. (Currently Amended) The method according to claim 74, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

76. (Original) The method according to claim 66, further comprising applying radiation of a type and in an amount effective to provide photodynamic therapy to the patient.

77. (Original) The method according to claim 76, wherein the radiation effective to provide photodynamic therapy is administered by an endoscope.

Claim 78 (Canceled)

79. (Currently Amended) The method according to claim [78] 77, wherein the ICG is provided at a concentration of at least 50 mg/ml.

80. (Original) The method according to claim 76, wherein step (e) comprises applying radiation of a type and in an amount sufficient to provide dye-enhanced photocoagulation as the dye enters the targeted tissue, and subsequently applying radiation of a type and in an amount to provide for PDT.

81. (Currently Amended) A method for reducing the rate of blood flow through a vessel that carries blood into a tumor of an animal comprising

(a) administering an aqueous ICG composition comprising ICG at a concentration of at least about [10] 20 mg/ml and an aqueous diluent comprising a solubilizer and an alcohol to a patient; and

(b) after the ICG dye enters the blood vessel that carries blood into the tumor, applying energy to the blood vessel of a type and in an amount sufficient to excite the ICG in the blood vessel and reduce the rate of blood flow through the vessel.

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wherein the ICG composition exhibits a loss of ICG potency of less than about 10% for at least 24 hours when stored in a 25°C environment.

82. (Original) The method according to claim 81, wherein step (b) comprises applying radiation as the dye entered the vessel of a type and in an amount sufficient to provide dye-enhanced photocoagulation of the vessel, and further comprising applying radiation to the tumor of a type and in an amount to provide PDT to the tumor.

83. (Original) The method of claim 81, wherein the radiation is administered in at least step (b) using an endoscope.

84. (Original) The method of claim 82, wherein the angiographic image is of tissue that defines a body cavity.

85. (Original) The method of claim 84, wherein the tissue is the eye, lung, gastrointestinal tract, bladder, pancreas, gall bladder, sinus, liver, trachea, kidney, heart, cervix, brain, ovary, prostate, stomach or skin.

86. (Original) The method according to claim 82, wherein the ICG is in the aqueous ICG composition at a concentration of at least 50 mg/ml.

87. (Currently Amended) The method according to claim 86, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

88. (Currently Amended) The method according to claim 87, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

89. (Original) The method according to claim 83, wherein the ICG is in the aqueous ICG composition at a concentration of at least 75 mg/ml.

90. (Currently Amended) The method according to claim 89, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 48 hours.

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91. (Currently Amended) The method according to claim 90, wherein the aqueous composition [is stable] exhibits a loss of ICG potency of less than about 10% for at least 7 days.

92. (Original) The method according to claim 82, further comprising applying radiation of a type and in an amount effective to provide photodynamic therapy to the patient.

93. (Original) The method according to claim 85, wherein the radiation effective to provide photodynamic therapy is administered by an endoscope.

94. (Original) The method according to claim 93, wherein the ICG is provided at a concentration of at least 25 mg/ml.

95. (Original) The method according to claim 93, wherein the ICG is provided at a concentration of at least 50 mg/ml.

96. (Original) The method according to claim 85, wherein the radiation effective to provide photodynamic therapy is administered by an endoscope.

97. (New) The composition according to claim 1, wherein the ICG composition comprises no more than about 1 wt.% degradation product when stored in the 25°C environment.

98. (New) The composition according to claim 5, wherein the ICG composition comprises no more than about 1 wt.% degradation product when stored in the 25°C environment.

99. (New) The composition according to claim 12, wherein the ICG composition comprises no more than about 1 wt.% degradation product when stored in the 25°C environment.

100. (New) The composition according to claim 18, wherein the ICG composition comprises no more than about 1 wt.% degradation product when stored in the 25°C environment.